

The possibility that the increase in the quantity of the lactic acid may likewise assist, if not be a material cause, in producing the nerve-symptoms, is also worthy of note.

That sugar, acting as sugar, was not their cause was shown by the symptoms not appearing until from a quarter to one hour after its injection. That is to say, not till the quantity of sugar present in the blood had already markedly decreased.

XVIII. "Experiments on Variola and Vaccinia." By S. MONCKTON COPEMAN, M.A., M.D. (Cantab.). Communicated by Professor M. FOSTER, Sec. R.S. Received June 14, 1893.

In the course of some experiments on the bacteriology of vaccine lymph, I was confronted by a difficulty in the practical testing of certain of the results of my work. Continuous experimentation on children being obviously out of the question, I was naturally led to turn my attention to the discovery if possible, of some one or more of the lower animals which, by reason of their passing through the various stages of vaccination and more especially variolation in a manner comparable with that witnessed in the human subject, might serve me for control experiments.

Little or no success having been obtained with the various domestic animals, I next turned to the monkey tribe on account of their similarity in many respects to man, although assured at the time that they were not susceptible to either vaccinia or variola. On putting the matter to the test, however, I found that this was not the case, the inoculation of vaccine and of variolous lymph having each of them given, in my hands, successful results in every instance in which I have tried it on the monkey (*Rhæsus*).

In the case alike of variola and of vaccinia, the local result of inoculation attains its acme (*quâ* vesiculation) in the monkey, as in the human being, about the eighth day. The first signs of reaction appear usually on the third day, by which time, if variolous lymph has been used, there is a distinct, though very thin, crust over the site of inoculation. By the fifth day vesiculation has generally commenced, this becoming more obvious up to the eighth day, though even then it is much less marked in variolous cases than in those which have been vaccinated, the difference being easily recognisable.

Later the vesicle gives rise to a pustule, by which time there is not infrequently considerable swelling of the skin and subcutaneous tissue and of the nearest lymphatic glands. The pustule gradually dries up, and a scab is formed which is more pronounced after vaccination than variolation, and which falls off some time during the third week, if the monkey has not picked it off before.

The chief difference noted between the effects resulting from the local inoculation of these two diseases, in the monkey, is that in the case of variola there is more or less of a crust from the first; that vesiculation is much less marked in variolation than in vaccination; that with variola about the ninth to the eleventh day a general eruption may appear which in some instances covers the whole surface of the body; and that the final scab at the site of inoculation is not so elevated in the variolated as in the vaccinated animal.

In both cases there is a rise of body temperature, which is more marked and longer sustained in variola than in vaccinia. After variolation it was noticed in several instances that the monkey suffered from diarrhoea, that its eyes were suffused, and that it was not as active as usual. A peculiar odour was also noticed, quite distinct from the well-known smell of "monkey."

In no instance had the disease a fatal termination.

It was next determined to make trial as to the protection against small-pox afforded in the monkey by previous vaccination, and the protection against vaccination afforded by variolation. And I went on to compare the effect produced by the use of human and of calf lymph respectively.

As the result of numerous experiments, it would appear that the mutually protective power of lymph obtained from the three different sources when inoculated on the monkey is practically identical in all respects.

Experiments have also been carried out on the bacteriology of vaccine lymph, with the view especially of discovering what means of storage are best adapted for securing sustained purity of the lymph and the unimpaired manifestation for indefinite periods of the action peculiar and essential to its use.

I have previously shown* that there are three species of micro-organisms, one or other, or all, of which is almost universally to be found in every specimen of vaccine lymph examined. These are (1) *Staphylococcus albus*, (2) *S. pyogenes aureus*, (3) *S. cereus flavus*; of which the first is frequently to be found in the upper layers of healthy skin. Numerous other bacteria occur from time to time, among which the *Staphylococcus pyogenes* deserves special mention.

These "extraneous" organisms flourish in the various nutrient media employed for cultivating purposes, and also in vaccine lymph itself when removed from the body, causing, by their exuberant growth, the opacity which sometimes occurs in old lymph stored in capillary tubes. It appeared, therefore, not unlikely that in this way the growth of the specific organism, if such exists, might be superseded.

Obviously, therefore, it was necessary to devise, if possible, some

* 'Transactions of International Congress of Hygiene,' 1891.

means of treating vaccine lymph which should inhibit all "extraneous" organisms without injuring its potency for vaccination. To this end I first made trial of the method of fractional heating as suggested by Kitasato for the isolation of the tetanus bacillus. Although apparently successful in many instances, the desirability speedily became apparent of some method of readier application and requiring less delicate manipulation.

This I at length found in the admixture with the lymph of a definite proportion of glycerine prior to storage in the usual way.

Not only is lymph thus treated efficient as vaccine in the old sense of the word, but as time goes on, instead of losing its effect on inoculation, its potency actually becomes increased. Experiment shows also that in tubes filled with such diluted lymph, opacity does not apparently result. As I have previously stated, the glycerine inhibits the growth of, and after a longer or shorter interval kills off altogether, those aërobic bacteria which I have termed "extraneous." This effect may be demonstrated by making, from tubes of glycerinated lymph of equal age, a series of plate cultivations at gradually increasing intervals of time, together with control cultivations from tubes of untreated lymph. These results have recently been entirely corroborated by Selavo, Chambon and Ménard, Straus, and other observers, such corroboration being the more valuable since it would appear that none of these observers were acquainted with the similar results at which I had previously arrived, and which were published* more than a year ago.

There can thus, I venture to think, be no doubt as to the superiority of the suggested method of lymph storage over the perhaps simpler method which up to the present time has been commonly employed in England. In Germany and elsewhere glycerine has been made use of for various reasons, but hitherto without knowledge, as far as I am aware, of the peculiar action exerted by it in the purification of the lymph.

The Society adjourned over the Long Vacation to Thursday, November 16.

Presents, June 15, 1893.

Transactions.

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* 'Transactions of the Epidemiological Society,' 1891-92.